REMARKS

Applicants elect with traverse Group 2, stable modification, and homologous recombination for examination on the merits. With regard to the requirements for an election of species, the following are elected:

(i) transcriptional level (claims 1-25 and 40-42 read on the elected species);

(ii) transverse aortic constriction (claims 1-9, 11-25 and 40-42 read on the elected species); and

(iii) 129SV (claims 1-25 and 40-42 read on the elected species).

Applicants reserve the right to prosecute non-elected subject matter in a further patent application.

Notwithstanding the above election, reconsideration of the restriction requirement is requested because examination of all pending claims would not constitute a serious burden. In particular, the claims of Groups 1-6 should be examined in the same application as they were in the Office Action mailed May 3, 2006. Thus, claims 19-23 should not be withdrawn from consideration.

In the alternative, Applicants disagree with the allegation in the Action that the pending claims lack unity of invention, and therefore belong to different groups of inventions. Applicants agrees that the inventions indicated by the Examiner are separately patentable. But traversal is based on the pending claims being so linked as to form a single general inventive concept under PCT Rule 13.1. Therefore, Applicants request that the pending claims be examined together in this application.

Applicants submit that, in accordance with the M.P.E.P., the claims identified by the Examiner as Groups 2, 4, 6, stable or transient modification of melusin expression, and different levels of regulating melusin expression are linked to form a single general inventive concept. In particular, the Examiner's attention is directed to M.P.E.P. § 1850 III. A. Combinations of Different Categories of Claims (8th Ed., Rev. 3, August 2005) which states at 1800-97 to 1800-98:

> The method for determining unity of invention under Rule 13 PCT shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application:

> (A) In addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product . . .
>
> [A] process shall be considered to be specially adapted for the manufacture of a product if the claimed process inherently results in the claimed product with the technical relationship being present between the claimed product and claimed process. The words "specially adapted" are not intended to imply that the product could not also be manufactured by a different process.

It was alleged in the Action that the inventions listed by the Examiner do not relate to a single general inventive concept because they lack the same special technical feature under PCT Rule 13.2. But here, the special technical feature linking the pending claims is that they all involve "a non-human transgenic animal having altered melusin expression" (note that the cells of claims 20-23 are derivable from that animal), which relates to the biological function of the melusin gene in such animals instead of the identification of the melusin gene itself. The latter was known when the claimed invention was filed in this patent application (see J. Biol. Chem. 279:29282-29288, 1999) and this was known to Applicants so it should be clear that the inventive concepts disclosed in their application underlie the pending claims instead of the prior art.

The generation of a non-human transgenic animal in which melusin gene expression was altered (Example 1 of the specification) made possible the discovery of the key role of melusin in triggering cardiomyocyte hypertrophy in response to stress stimuli such as pressure overload (Example 2 of the specification). The absence of melusin function in animals undergoing left ventricle dilation and failure upon pressure overload clearly demonstrated an important role of melusin in sustaining heart function in this pathological condition. In contrast, identification of melusin function would not have been possible from mere inspection of its gene and protein structures.

The general inventive concept providing unity of invention for the claims pending in this application is Applicants' innovation that functional melusin prevents cardiac dilation and heart failure. For this reason, Applicants strongly disagree with the arguments presented in the Action holding the claims of Groups 1, 3, 5 as distinct inventions from the claims of Groups 2, 4, 6 since decreasing or increasing melusin expression in a non-human transgenic animal are indeed different applications of the same inventive

concept (i.e., altering melusin expression). In particular, decreased melusin expression can be useful to generate heart failure animal or in vitro cellular models to test medicaments useful as therapeutic agents. On the other hand, increased melusin level can per se represent a therapeutic approach to treat heart failure.

An object of Applicants' invention is the practical application of their discovery of the role of melusin in cardiac function. This discovery was neither taught nor suggested by the prior art cited in the Action. In their specification, Applicants demonstrate that altering melusin expression causes reproducible physiological effects in the heart. This is a general inventive concept linking the claims of the groups of inventions indicated in the Action. Accordingly, Applicants submit that there is no lack of unity with regard to the pending claims.

Furthermore, claim 1 is a generic or linking claim in this application because "an increase" and "a decrease" are both alterations in melusin expression. Such alteration may be caused by a "stable" or "transient" modification. Additionally, claim 1 is a generic or linking claim for the genetic approaches for modifying melusin expression, the level at which melusin expression is controlled, the methods of inducing a hypertensive condition, and the strains of mice. Therefore, examination should proceed under the provisions of M.P.E.P. § 809.

Finally, it was alleged in the Action that "a proper search and examination cannot be carried out" on the pending claims. But this allegation contradicts the instruction to examiners in M.P.E.P. § 704.01 that "full faith and credit should be given to the search and action of the previous examiner unless there is a clear error in the previous action or knowledge of other prior art." Here, there is no evidence of either clear error or knowledge of other prior art. Even assuming for the sake of argument that multiple distinct inventions are claimed in this application, restriction is discretionary because a patent may contain such claims so the absence of a restriction requirement is not clear error. Therefore, the full faith and credit that should be given to the previous examiner's search prohibits restriction of the previously examined claims.

On October 27, 2006, the undersigned left a voicemail message for the Examiner to confirm that the next Action would not be made final in view of her allegation that the

claims were not properly searched and examined. The Examiner then left a voicemail message for the undersigned on October 30, 2006 confirming that a non-final Action would be mailed after receipt of this election.

Applicants earnestly solicit an early and favorable examination on the merits. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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By: _____

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